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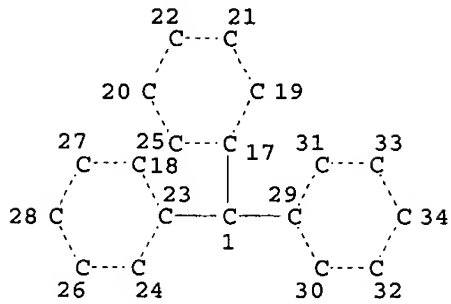
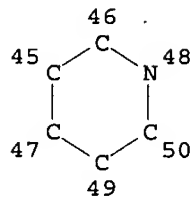
L9 STR





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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 48
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

=> s l9 ful
FULL SEARCH INITIATED 12:39:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 37588 TO ITERATE

100.0% PROCESSED 37588 ITERATIONS 1377 ANSWERS
SEARCH TIME: 00.00.01

L11 1377 SEA SSS FUL L9

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	150.95	222.85

FILE 'CAPLUS' ENTERED AT 12:39:59 ON 19 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 19 Jun 2003 VOL 138 ISS 25
FILE LAST UPDATED: 18 Jun 2003 (20030618/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L14           8 L13 AND MUSCARI?

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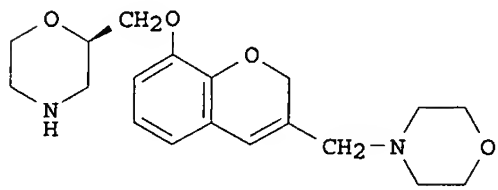
L14 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1998:269548 CAPLUS
DN 128:265746
TI (R)-(+)-2-[[[3-(Morpholinomethyl)-2H-chromen-8-yl]oxy]methyl]morpholine Methanesulfonate: A New Selective Rat 5-Hydroxytryptamine1B Receptor Antagonist
AU Berg, Stefan; Larsson, Lars-Gunnar; Renyi, Lucy; Ross, Svante B.; Thorberg, Seth-Olof; Thorell-Svantesson, Gun
CS Departments of Medicinal Chemistry Behavioral and Biochemical Pharmacology and Molecular Pharmacology, Preclinical RD, Soedertaelje, S-151 85, Swed.
SO Journal of Medicinal Chemistry (1998), 41(11), 1934-1942
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



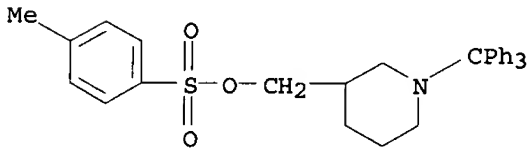
I

AB In the search for new 5-hydroxytryptamine (5-HT) receptor antagonists it was found that the compd. (R)-(+)-2-[[[3-(morpholinomethyl)-2H-chromen-8-yl]oxy]methyl]morpholine methanesulfonate [(R)-

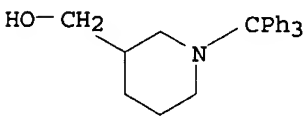
I.cntdot.MeSO3H.cntdot.H2O], is a selective rat 5-hydroxytryptamine1B (r5-HT1B) receptor antagonist. The binding profile showed a 6-fold preference for r5-HT1B (Ki = 47 .+-. 5 nM; n = 3) vs bovine 5-HT1B (Ki = 630 nM; n = 1) receptors. (R)-I.cntdot.MeSO3H.cntdot.H2O had very low affinity for other monoaminergic receptors examd. The r5-HT1B receptor antagonism was demonstrated by the potentiation of the K+-stimulated release of [3H]-5-HT from superfused rat brain slices in vitro, an effect that was antagonized by addn. of 5-HT to the superfusion fluid. (R)-I.cntdot.MeSO3H.cntdot.H2O at 20 mg/kg s.c. enhanced the 5-HT turnover in four rat brain regions (hypothalamus, hippocampus, striatum, and frontal cortex) with about 40% measured as the 5-HTP accumulation after decarboxylase inhibition with 3-hydroxybenzylhydrazine. At 3 mg/kg s.c. (R)-I.cntdot.MeSO3H.cntdot.H2O produced a significant increase in the no. of wet dog shakes in rats, a 5-HT2A/5-HT2C response that was abolished by depletion of 5-HT after pretreatment with the tryptophan hydroxylase inhibitor p-chlorophenylalanine. These observations show that (R)-I.cntdot.MeSO3H.cntdot.H2O, by inhibiting terminal r5-HT1B autoreceptors, increases the 5-HT turnover and the synaptic concn. of 5-HT.

IT **205242-47-3P**, 3-[(Tosyloxy)methyl]-1-tritylpiperidine
205242-48-4P, 1-Tritylpiperidine-3-methanol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of [(morpholinomethyl)chromen]oxy]methyl]morpholine mesylate as a 5-HT receptor antagonist)

RN 205242-47-3 CAPLUS
CN 3-Piperidinemethanol, 1-(triphenylmethyl)-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)



RN 205242-48-4 CAPLUS
CN 3-Piperidinemethanol, 1-(triphenylmethyl)- (9CI) (CA INDEX NAME)

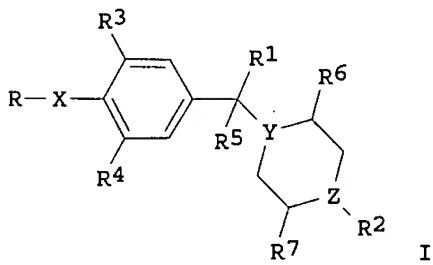


L14 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1998:112193 CAPLUS
DN 128:180426
TI Preparation of piperazine and piperidine derivatives as **muscarinic** antagonists
IN Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.; Berger, Joel G.; McQuade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-yong; Clader, John W.; Chackalamannil, Samuel; Wang, Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro, Wayne D.; Green, Michael J.; Browne, Margaret E.; Asberom, Theodros; Boyle, Craig D.; Josien, Hubert B.
PA Schering Corp., USA
SO PCT Int. Appl., 156 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9805292	A2	19980212	WO 1997-US13383	19970806	<--
	WO 9805292	A3	19980402			
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5889006	A	19990330	US 1996-700628	19960808	
	AU 9738999	A1	19980225	AU 1997-38999	19970806	<--
	AU 724001	B2	20000907			
	EP 938483	A2	19990901	EP 1997-936296	19970806	
	EP 938483	B1	20030226			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO					
	BR 9711119	A	19991123	BR 1997-11119	19970806	
	JP 2000501117	T2	20000202	JP 1998-508038	19970806	
	NZ 333801	A	20000428	NZ 1997-333801	19970806	
	AT 233260	E	20030315	AT 1997-936296	19970806	
	NO 9900551	A	19990407	NO 1999-551	19990205	
PRAI	US 1996-700628	A	19960808			
	US 1995-392697	B2	19950223			
	US 1995-457712	B2	19950602			
	US 1996-602403	A2	19960216			
	WO 1997-US13383	W	19970806			

OS MARPAT 128:180426
GI



I

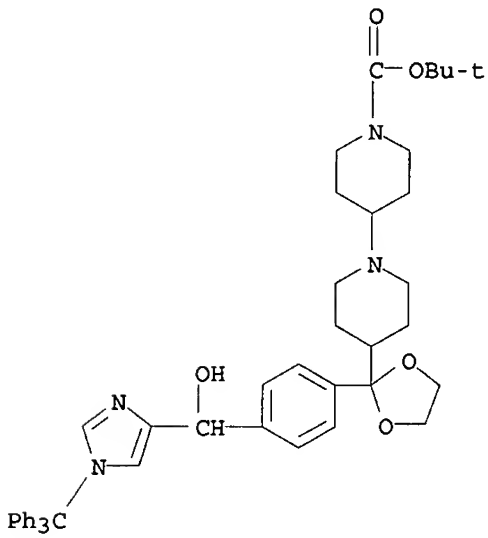
AB Title compds. I (R = OH, HOCH2, etc.; R1 = H, alkyl, alkenyl, cyano, etc.; R2 =H, (un)substituted piperidine; R3 = cycloalkylalkyl, haloacyl, benzyloxalkyl, etc.; R4 = H, halo, alkyl, alkoxy, etc.; R5 = H, alkyl,alkenyl,cyano, etc.; R1-R5 = (un)substituted satd. (hetero)cyclic ring; R6 = H, alkyl, hydroxyalkyl, arylalkyl, aminoalkyl, etc.; R7 = indolylalkyl, carboxyalkyl, etc.; X = O, S, SO, SO2,CO, CS, NHCOO, etc.; RX = I, Br, alkylcarbonyl, etc.; Y = N, CH, C-alkyl; Z = N, CH, C-alkyl), including isomers, salts, esters, and solvates, are prepd. and are defined **muscarinic** antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of prepn. are also disclosed. Also disclosed are synergistic combinations of I with acetylcholinesterase inhibitors.

IT **203185-77-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine and piperidine derivs. as **muscarinic** antagonists)

RN 203185-77-7 CAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4-[2-[4-[hydroxy[1-(triphenylmethyl)-1H-imidazol-4-yl]methyl]phenyl]-1,3-dioxolan-2-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1996:115120 CAPLUS

DN 124:175858

TI Preparation of heterocyclyl esters as **muscarine** M3 receptor antagonists

IN Takeuchi, Makoto; Naito, Makoto; Morihira, Koichiro; Ikeda, Masaru; Isomura, Yasuo

PA Yamanouchi Pharma Co Ltd, Japan

SO Jpn. Kokai Tokkyo Koho, 28 pp.
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 07258250	A2	19951009	JP 1994-56147	19940325 <--
PRAI JP 1994-56147		19940325		

OS MARPAT 124:175858

GI For diagram(s), see printed CA Issue.

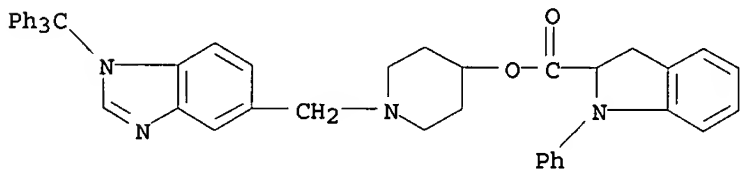
AB Heterocyclyl esters I [Y = single bond, CH2; p = 1, 2; q = 0, 1; provided that p + q = 1, 2; ring A = Q1, Q2, Q3; Z = NR1, NR3R2.Q-; Z1 = N, N+R3.Q-; Q- anion; m, n = 1, 2, 3, 4; provided that m + n = 3, 4, 5; l = 1, 2, 3; provided that m + l = 3, 4, 5; r, s, t = 0, 1, 2, 3; provided that r + s + t = 2, 3; R1 = H, alkyl, BR4; R2 = alkyl; R3 = alkyl, BR4; B = single bond, alkylene, alkenylene, alkynylene; R4 = (un)substituted heterocyclyl having 1 or 2 heteroatoms, Ph, indenyl, naphthyl] and their salts, useful as **muscarine** M3 receptor antagonists (no data), were prepd. Thus, refluxing Me 1-phenylindoline-2-carboxylate with 3-quinuclidinol and NaH in toluene for 2 h gave, after treatment with 4 N HCl in dioxane, 3-quinuclidinyl 1-phenylindoline-2-carboxylate

hydrochloride.

IT **173532-12-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclyl esters as **muscarine** M3 receptor antagonists)

RN 173532-12-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 2,3-dihydro-1-phenyl-, 1-[[1-(triphenylmethyl)-1H-benzimidazol-5-yl]methyl]-4-piperidinyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1995:994203 CAPLUS

DN 124:55800

TI Preparation of novel heterocyclyl pyridyl- or phenyl(methyl)carbamate derivatives as selective antagonists for **muscarine** M3 receptor

IN Takeuchi, Makoto; Naito, Ryo; Morihira, Koichiro; Hayakawa, Masahiko; Ikeda, Ken; Isomura, Yasuo

PA Yamanouchi Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9521820	A1	19950817	WO 1995-JP168	19950208 <--
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2182568	AA	19950817	CA 1995-2182568	19950208 <--
	AU 9515909	A1	19950829	AU 1995-15909	19950208 <--
	AU 685225	B2	19980115		
	EP 747355	A1	19961211	EP 1995-907855	19950208 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1140447	A	19970115	CN 1995-191543	19950208 <--
	HU 76289	A2	19970728	HU 1996-2188	19950208 <--
PRAI	JP 1994-16829		19940210		
	JP 1994-35064		19940304		
	JP 1994-102579		19940517		
	JP 1994-221335		19940916		
	JP 1994-267412		19941031		
	WO 1995-JP168		19950208		

OS MARPAT 124:55800

GI For diagram(s), see printed CA Issue.

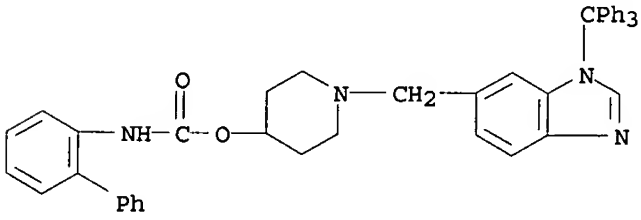
AB Carbamates derivs. represented by general formula [I; ring A = a benzene or pyridine ring; ring B = a satd. nitrogenous heterocycle which may be substituted on the nitrogen atom or cross-linked, i.e. Q - Q2; wherein Z = N(O)qR2, N+R3R4.A-; Z1 = N(O)q, N+R5.A-; wherein A- = anion; R2 = H, alkyl, alkenyl, alkynyl, cycloalkylalkyl, (un)substituted aralkyl,

heterocyclylalkyl having 1 or 2 heteroatoms and optional substituents on the heterocyclic ring and optionally condensed on the ring; R3 = alkyl, alkenyl, alkynyl, (un)substituted aralkyl, heterocyclylalkyl having 1 or 2 heteroatoms and optional substituents on the heterocyclic ring and optionally condensed on the ring; R4 = alkyl, alkenyl, alkynyl; R5 = alkyl, alkenyl, alkynyl, aralkyl; m, n = an integer of 1-4, provided that m + n = 3-5; p = an integer of 1-3; q = 0,1; r, s, t = an integer of 0-3, provided that r + s + t = 2 or 3; wherein R1 = optionally substituted Ph, C3-8 cycloalkyl or cycloalkenyl, or 5- or 6-membered nitrogenous heterocyclic group; X = a single bond or CH2; Y = a single bond, CO, optionally hydroxylated methylene, or -S(O)l; wherein l = an integer of 0, 1 or 2], salts, hydrates, or solvates thereof, useful for the treatment of prevention of digestive, respiratory or urol. diseases, are prepd. In particular, a remedy or preventive for chronic obstructive lung diseases, chronic bronchitis, asthma, rhinitis, nervous pollakiurea (frequent urination), nervous bladder, nocturnal enuresis, unstable bladder, bladder contracture, chronic cystitis, urinary incontinence, pollakiurea (frequent urination), irritable bowel syndrome, spasmodic colitis, or diverticulitis which is related to **muscarine** M3 receptor contains the said carbamate I as the active ingredient. Thus, 2.89 g (PhO)2P(O)N3 was added dropwise to a soln. of 1.98 g 2-biphenylcarboxylic acid and 1.11 g Et3N in 50 mL toluene, stirred at 60.degree. for 1.5 h, followed by adding 1.27 g 3-quinuclidinol, and the resulting mixt. was refluxed for 6 h to give, after workup and silica gel chromatog., 2.47 g 3-quinuclidinyl N-(2-biphenylyl)carbamate (II). The latter compd. (0.46 g) was stirred with MeI in 2-butanone at room temp. for 5.5 h to give 0.58 g 3-[[N-(2-biphenylyl)carbamoyl]oxy]-1-methylquinuclidinium iodide (III). II and III showed a binding affinity with the dissocn. const. Ki of 0.94 and 0.56 nM, resp., for **muscarine** M3 receptor prepn. from submaxillary gland membrane and that of 25.9 and 14.4 nM, resp., for **muscarine** M2 receptor prepn. from heart membrane and the binding affinity ratio of the **muscarine** M2 and M3 receptor was 27.6 and 25.7 for II and III, resp. II and III inhibited 50% the gallamine-induced contraction of a respiratory tract of guinea pig at 0.0045 and 0.0038 mg/kg i.v., resp., vs. 0.0008 mg/kg i.v. for atropine.

IT **171723-37-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel heterocyclyl pyridyl(methyl)- or phenyl(methyl)carbamate derivs. as selective antagonists for **muscarine** M3 receptor)

RN 171723-37-8 CAPLUS

CN Carbamic acid, [1,1'-biphenyl]-2-yl-, 1-[[1-(triphenylmethyl)-1H-benzimidazol-6-yl]methyl]-4-piperidinyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1995:849168 CAPLUS

DN 123:285789

TI Preparation of heterocyclyl carbamate derivatives with **muscarine** M3 receptor antagonism

IN Takeuchi, Makoto; Naito, Ryo; Morihira, Koichiro; Hayakawa, Masahiko; Ikeda, Ken; Isomura, Yasuo; Tomioka, Kenichi

PA Yamanouchi Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9506635	A1	19950309	WO 1994-JP1436	19940831 <--
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	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9475458	A1	19950322	AU 1994-75458	19940831 <--
PRAI	JP 1993-218620		19930902		
	JP 1994-77575		19940415		
	WO 1994-JP1436		19940831		

OS MARPAT 123:285789

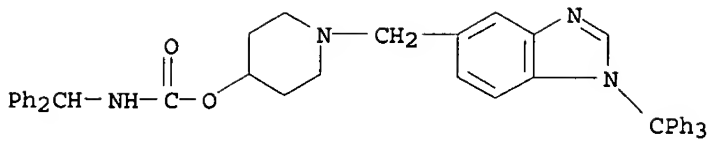
GI For diagram(s), see printed CA Issue.

AB Heterocyclyl (thio)carbamate and (thio)urea derivs. represented by general formula [I; R = (un)substituted aryl; R1 = cycloalkyl, (un)substituted aryl; R2 = H, OH, lower alkyl, lower alkoxy, cycloalkyl, aryl; R3 = H, lower alkyl; X = O, S; Y = O, S, (un)substituted NH, CH2, OCH2; ring A = heterocyclyl Q - Q1; wherein m, n = 1-4, provided that m + n = 3-5; l = 1-3, provided that m + l = 3-5; p, q = 0, 1; r, s, t = 0-3, provided that r + s + t = 2 or 3; Z = N(O)qR4, N+R5R6.Q-; Z1 = N(O)q, N+R6.Q-; wherein Q- = anion; R4 = H, lower alkyl, alkenyl, or alkynyl, B-R7; R5 = lower alkyl, alkenyl, or alkynyl, B-R7; R6 = lower alkyl, alkenyl, or alkynyl; wherein R7 = cycloalkyl, lower (hydroxy)alkoxy, benzhydryl, (un)substituted aryl, optionally benzene ring-fused or (un)substituted heterocyclyl contg. 1 or 2 heteroatoms; B = single bond, lower alkylene, alkenylene, or alkynylene] or salts, hydrates or solvates thereof are prepd. A **muscarine** M3 receptor antagonist for preventing or treating digestive tract, respiratory or urol. diseases such as irritable bowel syndrome, spasmodic colitis, diverticulitis, chronic obstructive lung diseases, chronic bronchitis, asthma, rhinitis, neural pollakiurea, nocturnal enuresis, nervous bladder, unstable bladder, bladder contracture, chronic cystitis, urinary incontinence, and pollakiurea, contains the said compd. I. Thus, 2.92 g NaBH(OAc)3 was added portion-wise to a soln. of 1.60 g 4-piperidyl N-benzhydrylcarbamate hydrochloride (prepn. given) and 0.40 mL 3-thiophenecarbaldehyde in 20 mL ClCH2CH2Cl and the resulting mixt. was stirred at room temp. overnight to give, after silica gel chromatog. and salt formation, a title compd. [II.(CO2H)2]. II.(CO2H)2 in vitro showed binding affinity to **muscarine** M1 receptor of cerebral cortex, **muscarine** M2 receptor of heart, and **muscarine** M3 receptor of submaxillary gland with Ki value of 1.0, 350, and 6.0 nM, resp., and Ki(M2 receptor)/Ki (M3 receptor) ratio of 58.

IT **168830-87-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for prepn. of heterocyclyl (thio)carbamate derivs. as **muscarine** M3 receptor antagonists)

RN 168830-87-3 CAPLUS

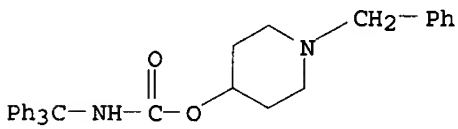
CN Carbamic acid, (diphenylmethyl)-, 1-[[1-(triphenylmethyl)-1H-benzimidazol-5-yl]methyl]-4-piperidinyl ester (9CI) (CA INDEX NAME)



IT **168829-14-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl (thio)carbamate derivs. as **muscarine** M3 receptor antagonists)
RN 168829-14-9 CAPLUS
CN Carbamic acid, (triphenylmethyl)-, 1-(phenylmethyl)-4-piperidinyl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

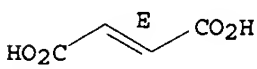
CRN 168829-13-8
CMF C32 H32 N2 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



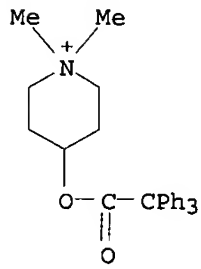
L14 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1995:531329 CAPLUS
DN 123:111884
TI Synthesis, **muscarinic** blocking activity and molecular modeling studies of 4-DAMP-related compounds
AU Recanatini, Maurizio; Tumiatti, Vincenzo; Budriesi, Roberta; Chiarini, Alberto; Sabatino, Piera; Bolognesi, Maria L.; Melchiorre, Carlo
CS Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy
SO Bioorganic & Medicinal Chemistry (**1995**), 3(3), 267-77
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
AB A no. of compds. structurally related to 4-DAMP [4-[(diphenylacetyl)oxy]-1,1-dimethylpiperidinium iodide] were synthesized and a single crystal X-ray structural study on a representative member of this series was carried out. All the compds. were tested for the antagonist activity in isolated guinea pig atria (M2 **muscarinic** receptors) and ileum (M3 **muscarinic** receptors). Affinity values (pA2) for the

muscarinic receptor subtypes ranged from 5.39 to 9.71 (M2) and from 5.68 to 9.92 (M3), depending on different structural features of the compds. A mol. modeling study was performed, with the aim of rationalizing the affinity data for both M2 and M3 **muscarinic** receptor subtypes. The presence in all the compds. could be fitted in a satisfactory manner.

IT **165613-34-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, **muscarinic** blocking activity, and mol. modeling studies of 4-DAMP-related compds.)

RN 165613-34-3 CAPLUS

CN Piperidinium, 1,1-dimethyl-4-[(triphenylacetyl)oxy]-, iodide (9CI) (CA INDEX NAME)

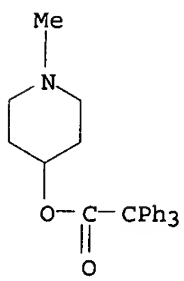


● I^-

IT **165613-28-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, **muscarinic** blocking activity, and mol. modeling studies of 4-DAMP-related compds.)

RN 165613-28-5 CAPLUS

CN Benzeneacetic acid, .alpha.,.alpha.-diphenyl-, 1-methyl-4-piperidinyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1987:95583 CAPLUS

DN 106:95583

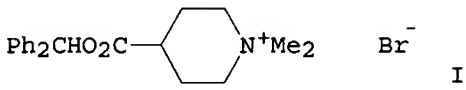
TI A further search for selective antagonists at M2-**muscarinic** receptors

AU Barlow, R. B.; Shepherd, M. K.

CS Med. Sch., Univ. Walk, Bristol, BS8 1TD, UK

SO British Journal of Pharmacology (**1986**), 89(4), 837-43

CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
GI

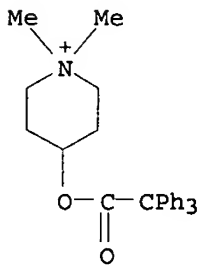


I

AB In an attempt to obtain more selective antagonists acting at **muscarinic** M2-receptors, 26 analogs of 4-diphenylacetoxy-N-methylpiperidine methobromide (4-DAMP methobromide) (I) were synthesized. These were tested, along with silabenzhexol, procyclidine, sila-procyclidine and AFDX-116, in concn.-ratio expts. with guinea pig isolated atria at 30.degree. and ileum at 30.degree. and 37.degree.. The agonist was carbachol and the selectivity was assessed from the difference between log K for receptors in the ileum and log K for receptors in the atria. The selectivity was not related to the affinity, and some weakly active compds. retained appreciable selectivity, but no compd. had greater selectivity than 4-DAMP methobromide. Structure-activity relations are discussed. There seem to be steric limits to affinity but there are no obvious indications of the structural features assocd. with selectivity. It is suggested that more selective drugs may be obtained by introducing groups which may reduce affinity.

IT **106618-70-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **muscarinic** M2 receptor antagonist)

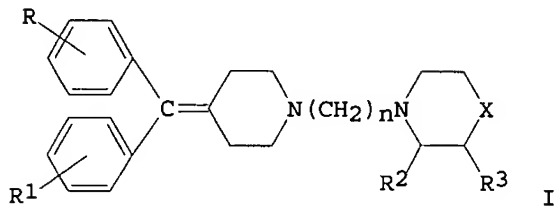
RN 106618-70-6 CAPLUS
CN Piperidinium, 1,1-dimethyl-4-[(triphenylacetyl)oxy]-, bromide (9CI) (CA INDEX NAME)



L14 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1986:168368 CAPLUS
DN 104:168368
TI Diphenylmethylenepiperidines
IN Downs, David A.; Tecle, Haile
PA Warner-Lambert Co. , USA
SO U.S., 19 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4540780	A	19850910	US 1983-500344	19830602 <--
	US 4584301	A	19860422	US 1985-734432	19850516 <--
	US 4640925	A	19870203	US 1986-828377	19860211 <--
	US 4666905	A	19870519	US 1986-905214	19860909 <--
PRAI	US 1983-500344		19830602		
	US 1985-734432		19850516		
	US 1986-828377		19860211		
OS	CASREACT 104:168368				

GI



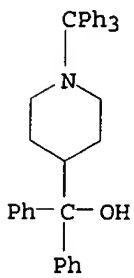
I

AB The title compds. I [R, R1 = H, halogen, halomethyl, alkyl, alkoxy; R2, R3 = H, alkyl, (hetero)aryl; X = bond, O, CH2, S, CHOH, CHCH2CH2OH, C(OH)2, NR4; R4 = H, alkyl, aryl; n = 2-4], having both anticholinergic and antidopaminergic properties, were prepd. Thus, 0.05 mol Et isonipecotate was treated with 0.05 mol N-(2-chloroethyl)morpholine-HCl to give Et 1-[2-(4-morpholinyl)ethyl]-4-piperidinecarboxylate (quant. yield), which was treated with 0.30 mol PhLi to give 1-[2-(4-morpholinyl)ethyl]-.alpha.,.alpha.-diphenyl-4-piperidinemethanol. The latter compd. was treated with 10% HCl at reflux to give 77% I-2HCl (R = R3 = H, n = 2) (II), which inhibited quinuclidinyl benzilate binding by **muscarinic** cholinergic receptors in rat brain and haloperidol binding by dopamine receptors in rat brain with IC50 of 148 nM and 29 mM, resp. II also showed significant antiemetic properties in the apomorphine emesis assay with an ED50 .apprx.5.0 mg/kg, orally in dogs. A syrup contg. 250 mg II/5 mL was prepd. by dissolving 25 g II in 200 mL purified H2O and adding cherry syrup, q.s. to 1000 mL.

IT **101477-20-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and dehydration-detritylation of)

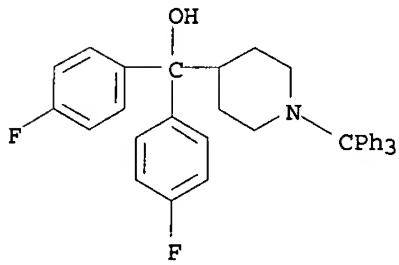
RN 101477-20-7 CAPLUS

CN 4-Piperidinemethanol, .alpha.,.alpha.-diphenyl-1-(triphenylmethyl)- (9CI) (CA INDEX NAME)

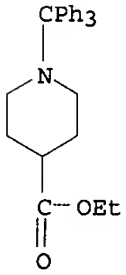


IT **101477-28-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. and detritylation of)
RN 101477-28-5 CAPLUS
CN 4-Piperidinemethanol, .alpha.,.alpha.-bis(4-fluorophenyl)-1-(triphenylmethyl)- (9CI) (CA INDEX NAME)



IT **81270-31-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with phenyllithium)
RN 81270-31-7 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-(triphenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



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L17           2 L16 AND MUSCARI?

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L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
AN   1999:581384  CAPLUS
DN   132:12269
TI   Synthesis and antagonistic activity at muscarinic receptor
     subtypes of some 2-carbonyl derivatives of diphenidol
AU   Varoli, L.; Angeli, P.; Burnelli, S.; Marucci, G.; Recanatini, M.
CS   Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Bologna,
     Bologna, 40126, Italy
SO   Bioorganic & Medicinal Chemistry (1999), 7(9), 1837-1844
     CODEN: BMECEP; ISSN: 0968-0896
PB   Elsevier Science Ltd.
DT   Journal
LA   English
AB   A series of 2-carbonyl analogs of the muscarinic antagonist
     diphenidol bearing 1-substituents of different lipophilic, electronic, and
     steric properties was synthesized, and their affinity for the M2 and M3
     muscarinic receptor subtypes was evaluated by functional tests.
     Two derivs. showed an M2-selective profile, which was confirmed by
     functional tests on the M1 and M4 receptors.  A possible relationship
     between M2 selectivity and lipophilicity of the 1-substituent was
     suggested by structure-activity anal.  This work showed that appropriate
     structural modification of diphenidol can lead to M2-selective
     muscarinic antagonists of possible interest in the field of
     Alzheimer's disease.
RE.CNT  26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS
AN   1998:112193  CAPLUS
DN   128:180426
TI   Preparation of piperazine and piperidine derivatives as muscarinic
     antagonists
IN   Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.; Berger, Joel G.;
     McQuade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar,
     Sundeep; Chen, Lian-yong; Clader, John W.; Chackalamannil, Samuel; Wang,
     Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro,
     Wayne D.; Green, Michael J.; Browne, Margaret E.; Asberom, Theodros;
     Boyle, Craig D.; Josien, Hubert B.
PA   Schering Corp., USA
SO   PCT Int. Appl., 156 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 4
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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     WO 9805292          A3   19980402
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             NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU,
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            GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
            GN, ML, MR, NE, SN, TD, TG
    US 5889006        A    19990330       US 1996-700628    19960808 <--
    AU 9738999        A1   19980225       AU 1997-38999     19970806
    AU 724001         B2   20000907
    EP 938483         A2   19990901       EP 1997-936296    19970806 <--
    EP 938483         B1   20030226
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
            LT, LV, FI, RO
    BR 9711119        A    19991123       BR 1997-11119     19970806 <--
    JP 2000501117     T2   20000202       JP 1998-508038    19970806
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    AT 233260         E    20030315       AT 1997-936296    19970806
    NO 9900551        A    19990407       NO 1999-551       19990205 <--
PRAI US 1996-700628   A    19960808
    US 1995-392697    B2   19950223
    US 1995-457712    B2   19950602
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OS  MARPAT 128:180426
GI
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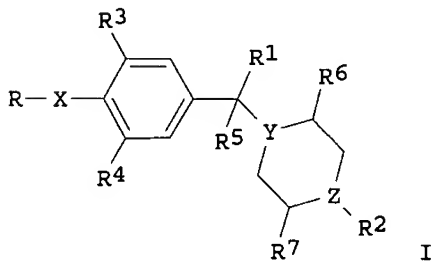

I

AB Title compds. I (R = OH, HOCH2, etc.; R1 = H, alkyl, alkenyl, cyano, etc.; R2 =H, (un)substituted piperidine; R3 = cycloalkylalkyl, haloacyl, benzyloxalkyl, etc.; R4 = H, halo, alkyl, alkoxy, etc.; R5 = H, alkyl,alkenyl,cyano, etc.; R1-R5 = (un)substituted satd. (hetero)cyclic ring; R6 = H, alkyl, hydroxyalkyl, arylalkyl, aminoalkyl, etc.; R7 = indolylalkyl, carboxyalkyl, etc.; X = O, S, SO, SO2,CO, CS, NHCOO, etc.; RX = I, Br, alkylcarbonyl, etc.; Y = N, CH, C-alkyl; Z = N, CH, C-alkyl), including isomers, salts, esters, and solvates, are prepd. and are defined **muscarinic** antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of prepn. are also disclosed. Also disclosed are synergistic combinations of I with acetylcholinesterase inhibitors.


```
=> d hitstr 1

L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
IT   251347-79-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (synthesis and antagonistic activity at muscarinic receptor
        subtypes of diphenidol derivs.)
RN   251347-79-2  CAPLUS
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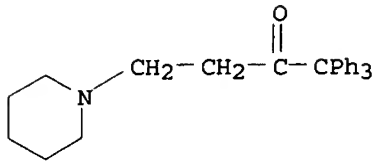
CN 2-Butanone, 1,1,1-triphenyl-4-(1-piperidinyl)-, hydrochloride (9CI) (CA INDEX NAME)



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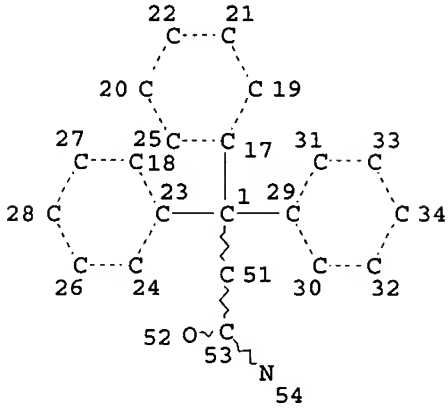

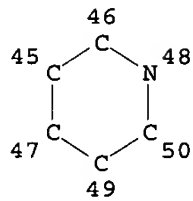

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DEFAULT ECLEVEL IS LIMITED

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RSPEC 48
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	149.75	427.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.51

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FILE COVERS 1907 - 19 Jun 2003 VOL 138 ISS 25
FILE LAST UPDATED: 18 Jun 2003 (20030618/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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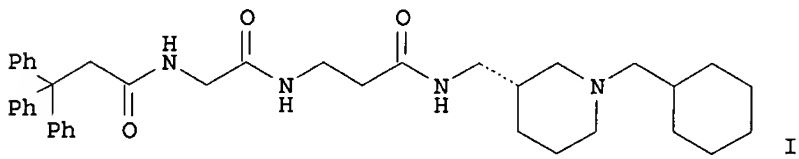
L21 2 L20

=> d bib abs 1-2

L21 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2002:54472 CAPLUS
DN 136:256738
TI Cyclohexylmethylpiperidinyltriphenylpropioamide: a selective muscarinic M3 antagonist discriminating against the other receptor subtypes
AU Sagara, Yufu; Sagara, Takeshi; Mase, Toshiaki; Kimura, Toshifumi; Numazawa, Tomoshige; Fujikawa, Toru; Noguchi, Kazuhito; Ohtake, Norikazu
CS Banyu Tsukuba Research Institute in collaboration with Merck Research Laboratories, Tsukuba, Ibaraki, 300-2611, Japan
SO Journal of Medicinal Chemistry (2002), 45(4), 984-987
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I

AB To discover a highly selective M3 antagonist, a combinatorial library was prepd. The library was designed to identify a novel structural class of M3 antagonists by exploring the spatial arrangement of the pharmacophores in known M3 antagonists. After the evaluation of 1000 library members, a potent M3 antagonist, (I) (Ki = 0.31 nM), with novel structural features was identified. Compd. I showed high selectivity for M3 receptors over the other muscarinic receptor subtypes (M1/M3 = 380-fold, M2/M3 = 98-fold, M4/M3 = 45-fold, M5/M3 = 120-fold).
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2001:78358 CAPLUS
DN 134:147498

TI Preparation of amide derivatives as selective muscarinic M3 antagonists

IN Sagara, Yufu; Uchiyama, Minaho; Naya, Akira; Kimura, Toshifumi; Numazawa, Tomoshige; Fujikawa, Toru; Otake, Norikazu; Noguchi, Kazuhito

PA Banyu Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001007406	A1	20010201	WO 2000-JP4762	20000714
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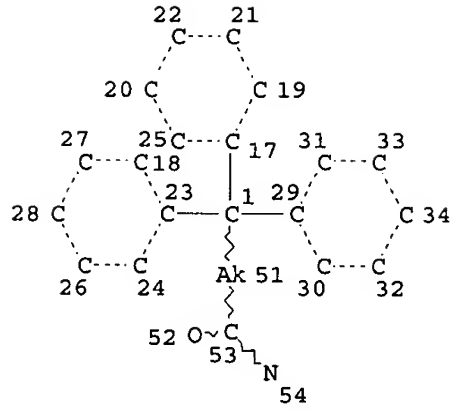
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1213281	A1	20020612	EP 2000-946352	20000714
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

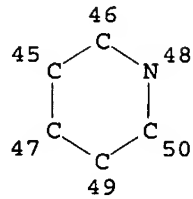
PRAI JP 1999-209292 A 19990723
JP 1999-338617 A 19991129
WO 2000-JP4762 W 20000714

OS MARPAT 134:147498

AB The title compds. Ar1C(Ar2)(Ar3)CHR1CON(R2)CHR3(CH2)pXY(R4)CHR5(CH2)mCONH(CH2)nA [A is piperidine moiety (generic structure given), etc.; Ar1, Ar2 and Ar3 are each optionally substituted phenyl; p is 0 or 1; m, n are each 0, 1 or 2 ; R1 is hydrogen or optionally substituted lower alkyl; R2, R3, R4 and R5 are each hydrogen, optionally substituted lower alkyl, or the like; X is carbonyl or methylene; Y is nitrogen or methine] are prepd. The title compds. are useful as remedies for respiratory, urol. or digestive diseases. In in vitro tests for M3 antagonism, compds. of this invention showed the Ki values of 1.3 nM to 4.7 nM; in in vitro tests for M1 and M2 antagonism, said compds. showed the Ki values of 110 nM to > 2500 nM.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT



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PROJECTED ANSWERS:                3 TO      255

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SEARCH TIME: 00.00.02

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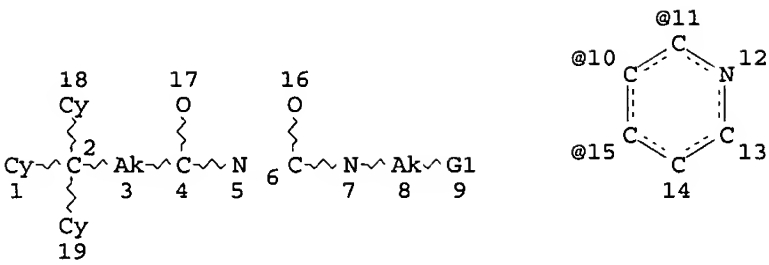
L1 HAS NO ANSWERS
L1 STR



VAR G1=10/11/15
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY AT 1
GGCAT IS MCY AT 18
GGCAT IS MCY AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 10
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

=> d his

(FILE 'HOME' ENTERED AT 12:22:53 ON 19 JUN 2003)

FILE 'REGISTRY' ENTERED AT 12:22:58 ON 19 JUN 2003
L1 STRUC
L2 0 S L1
L3 STRUC
L4 0 S L3
BATCH L1 CC31716/B SSS FUL

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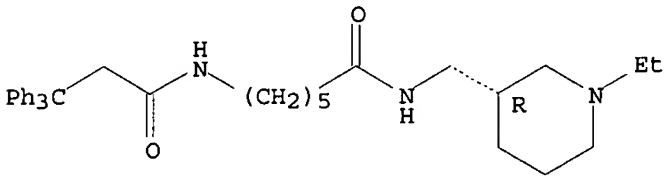
=> activate cc31716/a
L3              STR
L4           55 SEA FILE=REGISTRY SSS FUL L3

=> d scan

L4   55 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   Benzenepropanamide, N-[6-[[[(3R)-1-ethyl-3-piperidinyl]methyl]amino]-6-
     oxohexyl]-.beta.,.beta.-diphenyl- (9CI)
MF   C35 H45 N3 O2

Absolute stereochemistry.
```

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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=> s l4
L5            2 L4

=> d bib abs 1-2

L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
AN   2002:54472  CAPLUS
DN   136:256738
TI   Cyclohexylmethylpiperidinyltriphenylpropioamide: a selective muscarinic M3
     antagonist discriminating against the other receptor subtypes
AU   Sagara, Yufu; Sagara, Takeshi; Mase, Toshiaki; Kimura, Toshifumi;
     Numazawa, Tomoshige; Fujikawa, Toru; Noguchi, Kazuhito; Ohtake, Norikazu
CS   Banyu Tsukuba Research Institute in collaboration with Merck Research
     Laboratories, Tsukuba, Ibaraki, 300-2611, Japan
SO   Journal of Medicinal Chemistry (2002), 45(4), 984-987
     CODEN: JMCMAR; ISSN: 0022-2623
PB   American Chemical Society
DT   Journal
LA   English
GI
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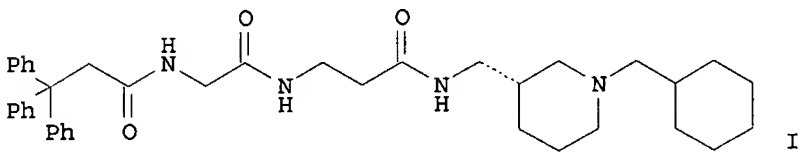

I

AB   To discover a highly selective M3 antagonist, a combinatorial library was prepd. The library was designed to identify a novel structural class of M3 antagonists by exploring the spatial arrangement of the pharmacophores in known M3 antagonists. After the evaluation of 1000 library members, a potent M3 antagonist, (I) (Ki = 0.31 nM), with novel structural features was identified. Compd. I showed high selectivity for M3 receptors over the other muscarinic receptor subtypes (M1/M3 = 380-fold, M2/M3 = 98-fold, M4/M3 = 45-fold, M5/M3 = 120-fold).


```
RE.CNT  25    THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS
AN   2001:78358  CAPLUS
DN   134:147498
TI   Preparation of amide derivatives as selective muscarinic M3 antagonists
IN   Sagara, Yufu; Uchiyama, Minaho; Naya, Akira; Kimura, Toshifumi; Numazawa,
     Tomoshige; Fujikawa, Toru; Otake, Norikazu; Noguchi, Kazuhito
PA   Banyu Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 187 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 2001007406      A1    20010201      WO 2000-JP4762   20000714
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
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LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1213281 A1 20020612 EP 2000-946352 20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

PRAI JP 1999-209292 A 19990723
JP 1999-338617 A 19991129
WO 2000-JP4762 W 20000714

OS MARPAT 134:147498

AB The title compds. Ar1C(Ar2)(Ar3)CHR1CON(R2)CHR3(CH2)pXY(R4)CHR5(CH2)mCONH(CH2)nA [A is piperidine moiety (generic structure given), etc.; Ar1, Ar2 and Ar3 are each optionally substituted phenyl; p is 0 or 1; m, n are each 0, 1 or 2 ; R1 is hydrogen or optionally substituted lower alkyl; R2, R3, R4 and R5 are each hydrogen, optionally substituted lower alkyl, or the like; X is carbonyl or methylene; Y is nitrogen or methine] are prepd. The title compds. are useful as remedies for respiratory, urol. or digestive diseases. In in vitro tests for M3 antagonism, compds. of this invention showed the Ki values of 1.3 nM to 4.7 nM; in in vitro tests for M1 and M2 antagonism, said compds. showed the Ki values of 110 nM to > 2500 nM.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT